Assessment of the Significance and Clinical Implications of Stress Hormones in Acute Pressure Injuries Among Trauma Patients

Haishuang Wang, MM; Hongbo Xu, MM; Huanle Shu, MM; Shi Xu, MM; Wei Wang, MD

ABSTRACT

Objective • This study examines the dynamic changes of stress hormones, including insulin (INS), fasting blood glucose (FBG), glucagon (Glu), and cortisol (Cort), in trauma patients. By monitoring these changes and observing acute pressure injury (API) occurrences on the skin, the research analyzes the influence of stress hormones on API development in trauma patients.

Methods • A prospective analysis involved 218 trauma patients admitted to a grade III-A general hospital in Wenzhou from April 2021 to June 2023. Among them, 44 cases developed API (API group), and 174 cases did not (control group). Levels of INS, Cort, Glu, and FBG were measured in both groups. Additionally, Abbreviated Injury Scale-Injury Severity Score (AIS-ISS) surveys and API severity assessments were conducted. Correlations between stress hormone levels and AIS-ISS were discussed. The predictive effects of AIS-ISS and stress hormones on API occurrence in trauma patients were analyzed using receiver operating characteristic (ROC) curves. The relationship between stress hormone levels and API severity was also observed.

Results • Study’s outcomes indicated distinct relationships between stress hormone levels and API occurrence in trauma patients. Specifically, INS demonstrated a negative correlation with AIS-ISS, highlighting its potential as a significant factor. Glu, Cort, and FBG revealed positive associations, emphasizing their roles in influencing API development (P < .05). The diagnostic efficacy of stress hormones in predicting API occurrence, as represented by the Area Under Curve (AUC) = 0.8100. Notably, within the API group, INS levels demonstrated a decline with worsening API. Conversely, Glu, Cort, and FBG exhibited increases in tandem with the aggravation of API symptoms (P < .05).

Conclusions • This research suggests that assessing stress hormone levels in clinical settings can effectively predict API occurrence. Early testing could aid in the development of preventive or intervention measures, reducing the incidence and harm of API in trauma patients. (Altern Ther Health Med. [E-pub ahead of print.])

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INTRODUCTION

Pressure injury (PI) is localized damage to the skin and subcutaneous tissue caused by intense and/or prolonged pressure, often combined with shear force. This type of injury is commonly found at bony prominences.1 Clinically, PI mostly occurs in areas of the skin that come into contact with medical devices like positive pressure ventilation masks and oxygen saturation probes.2 PIs are generally medical and localized injuries to the skin or cartilaginous tissues, presenting as either intact skin or open ulcers that may be associated with pain.3

Soft tissue tolerance to pressure and shear can be influenced by various factors, including the microenvironment, nutrition, perfusion, comorbidities, and the overall condition of the soft tissues.4 Clinical statistics reveal that severe trauma patients face a 9.20%-17.27% risk of developing API due to the combined effects of metabolic disorders and consumptive states.5 The occurrence of API not only extends the recovery period for patients but may also lead to additional complications, ultimately contributing to a poorer prognosis.6

Currently, the Braden risk assessment scale7 is widely employed as an assessment tool for clinical practice. However, its validity in the trauma population has been questioned, as it struggles to accurately quantify the API risk in trauma patients.2,8 Furthermore, the majority of current research on
This study prospectively analyzed 218 trauma patients admitted to a grade III-A general hospital in Wenzhou between April 2021 and June 2023. All patients underwent mechanical operations, such as mechanical ventilation and endotracheal intubation, at our hospital or required prolonged bed rest. Among them, 44 patients developed API and constituted the API group, while the remaining 174 patients without API formed the control group. The Ethics Committee of our hospital approved this study, and all subjects provided informed consent forms. Additionally, we conducted the study in strict adherence to the Declaration of Helsinki.

Criteria for Patient Enrollment and Exclusion

Inclusion criteria were as follows: (1) Patients aged 18 years or older with provided informed consent; (2) Braden risk assessment scale [7] score of ≤18; (3) Hospitalization time of ≥7 days; (4) Presence of a pressure injury identified after 24 hours of admission; (5) No history of pressure injury or skin changes; (6) Individuals requiring emergency surgery. Exclusion criteria were as follows: (1) Patients with acute/chronic skin diseases or burns; (2) Those with unstable vital signs or deemed unable to be followed up; (3) Presence of a pressure injury identified 6 days after surgery; (4) Individuals who had used protective dressing at the observation site upon admission; (5) Patients with a Braden scale score >18 points during the follow-up.

Grading Criteria

Abbreviated Injury Scale-Injury Severity Score (AIS-ISS). The trauma severity of all patients was scored using AIS-ISS. [16] The body was divided into six zones, and the maximum AIS value was selected from each of the three largest zones. The chosen values were squared and added, resulting in a total score. Scores of ≥15, ≥25, and ≥35 were classified as severe, critical, and extremely critical, respectively.

National Pressure Ulcer Advisory Panel (NPUAP) Criteria (2016). API patient injury severity was assessed as follows: [16] (1) Stage 1: Constant erythema without whitening after acupressure, with intact skin; (2) Stage 2: Partial cortical loss and dermal exposure, without exposure of adipose or deep tissue. The wound is pink/red, active, and moist, with a complete or broken serous blister; (3) Stage 3: Complete cortical skin loss with visible fat, granulation tissue, and edge involution; (4) Stage 4: Full-thickness skin and tissue loss, with visible fascia, muscles, tendons, ligaments, cartilage, or bone, either visible or directly palpable.

Sample Collection and Testing

Fasting elbow vein blood was obtained from all patients on the day of admission. Subsequently, the serum was centrifuged after allowing it to rest at room temperature. This process aimed to determine the levels of INS, Cort, Glu, and FBG using an automatic biochemical analyzer. After 7 days of treatment, additional blood samples were collected to measure the aforementioned indicators.

Outcome Measures

The study assessed the correlation between stress hormone levels and AIS-ISS. Additionally, the predictive effects of AIS-ISS and stress hormones on the occurrence of API in trauma patients were analyzed using receiver operating characteristic (ROC) curves. Finally, the study observed the relationship between stress hormone levels and API severity, along with changes in stress hormone levels before and after treatment.
Statistical Analyses

Data analyses were conducted using SPSS 24.0, and statistical significance was determined by a $P < .05$. Counting data, expressed as [$n$ (%)], underwent analysis using the chi-square test. Measurement data, described statistically as mean ± standard deviation ($\bar{x} \pm s$), were compared between groups using the independent samples $t$ test. Correlations were examined using Spearman correlation coefficients. The Log(P) of the joint detection curve was established through logistic binary regression analysis, and the predictive effect was evaluated using ROC curves. The closer the area under the curve (AUC) was to 1, the higher the authenticity of the detection method.

RESULTS

Comparison of Clinical Baseline Data

Upon an initial inter-group examination of patients’ clinical baseline data, no significant differences were observed in age, sex, trauma type, and other relevant factors ($P > .05$) as presented in Table 1.

Relationship between Stress Hormones and Trauma Severity

Through Spearman correlation coefficient analysis, we observed an inverse association between INS and trauma severity in both the control and API groups ($P < .05$). This implies that higher AIS-ISS values are linked to lower INS levels. Conversely, levels of Glu, Cort, and FBG showed positive correlations with the severity of trauma ($P < .05$). In other words, elevated AIS-ISS scores are associated with higher Glu, Cort, and FBG levels, see Figure 1.

Evaluation of the Braden Scale's Impact on API

The Braden scale score for the API group was (11.91 ± 3.08), significantly higher compared to the control group ($P < .05$). According to ROC analysis, the optimal cut-off for the Braden score was found to be <13.50, providing a sensitivity of 72.73%, specificity of 67.82%, and an AUC of 0.7599 for predicting the occurrence of API in trauma patients ($P < .05$), see Figure 2.

Evaluation of the Impact of Stress Hormones on API

In comparison with the control group, API patients exhibited a decrease in INS levels, while levels of Glu, Cort, and FBG were all elevated ($P < .05$). Logistic regression analysis yielded the joint detection formula $\log(P) = 3.555 + (-0.466 \times \text{INS}) + (-0.020 \times \text{Cort}) + (0.104 \times \text{Glucagon}) + (-0.433 \times \text{FBG})$ for INS, Glu, Cort, and FBG. ROC curves demonstrated that the combined formula (cut-off > 0.1144) had a predictive sensitivity of 93.18%, specificity of 56.90%, and an AUC of 0.8100 for the occurrence of API in trauma patients ($P < .05$). In comparison to the Braden score, stress hormones exhibited a significantly higher AUC for predicting the development of APIs in trauma patients, suggesting superior diagnostic efficacy, see Figure 3.

Table 1. Comparison of Clinical Baseline Data

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (± SD)</th>
<th>Sex</th>
<th></th>
<th>Types of Traumas</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group (n=174)</td>
<td>53.57±14.12</td>
<td>Male</td>
<td>99 (56.90)</td>
<td>Vehicle Accident</td>
<td>75 (43.10)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Fall</td>
<td>24 (13.79)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Burns</td>
<td>46 (26.44)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td>6 (3.45)</td>
</tr>
<tr>
<td>API Group (n=44)</td>
<td>54.70±10.65</td>
<td>Male</td>
<td>26 (59.09)</td>
<td>Vehicle Accident</td>
<td>28 (40.91)</td>
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<td></td>
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<td>Female</td>
<td>18 (40.91)</td>
<td>Strike</td>
<td>24 (54.55)</td>
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<td></td>
<td></td>
<td>Fall</td>
<td>8 (18.18)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Burns</td>
<td>9 (20.45)</td>
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<td></td>
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<td></td>
<td></td>
<td>Other</td>
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$P$ value

<table>
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<th>API Group</th>
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</thead>
<tbody>
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<td>0.621</td>
<td>0.069</td>
</tr>
<tr>
<td>3.054</td>
<td>0.549</td>
</tr>
</tbody>
</table>

Figure 1. Relationship between Stress Hormones and Trauma Severity. (A) Correlation of Stress Hormones and AIS-ISS Scores in the Control Group; (B) Correlation of Stress Hormones and AIS-ISS Scores in the API Group.

Note: The figures depict the correlation analysis between stress hormones and trauma severity in both the control and API groups.

Abbreviation: AIS-ISS, Abbreviated Injury Scale-Injury Severity Score.

Figure 2. Comparison of Braden Scores in the Control and API Groups and Evaluation Effect of the Braden Scale on API.

Note: The figure illustrates the comparison of Braden scores between the control and API groups, along with an assessment of the Braden scale's effectiveness in predicting API occurrence.

Figure 3. Comparison of Stress Hormones in the Control and API Groups and Evaluation Effect of Stress Hormones on API.

Note: The figure presents a comparative analysis of stress hormone levels between the control and API groups, along with an assessment of the impact of stress hormones on API occurrence.

Correlation between Stress Hormones and API

Similarly, Spearman correlation coefficient analysis revealed an inverse association between INS and the severity
DISCUSSION

In recent years, significant attention has been devoted to exploring indicators that describe the intensity of traumatic stress responses and analyzing their correlations with the occurrence of API. Past research has confined these relationships without providing guidance on risk quantification. Our study reveals that the occurrence of API can be effectively evaluated using stress response indexes specifically under severe trauma conditions suggesting the correlation between stress response and API occurrence. This finding not only strengthens the understanding of their relationship but also offers a reliable reference for early API prevention in the future.

Our study revealed a significant correlation of INS, Glu, Cort, and FBG with AIS-ISS in all trauma patients. This finding underscores the pivotal clinical role that stress hormones play in the pathological progression of trauma, aligning with prior studies. This correlation arises from the automatic activation of the body's stress response and neuroendocrine system post-trauma, leading to increased release of hormones such as adrenaline and cortisol, along with alterations in BG and INS regulation, aimed at coping with the stress induced by trauma. Subsequent API evaluation using the Braden scale exhibited an AUC of 0.7599, indicating an ordinary evaluation effect, reinforcing the consistency of our earlier observations.

The limitation of the Braden scale stems from its primary evaluation criteria, which center around the patient’s activities, nutrition, and other conditions. However, it lacks any assessment content specifically addressing stress responses. Consequently, the Braden scale may not be optimally suited for trauma patients experiencing significant stress responses. In our subsequent analysis, a comparison of stress hormone levels between the two groups revealed a decline in INS levels within the API group, coupled with increased levels of Glu, Cort, and FBG. This observation strongly suggests a close and intricate relationship between stress hormones and the occurrence of API.

Furthermore, the combined detection of INS, Glu, Cort, and FBG exhibited outstanding predictive efficacy for the occurrence of API in trauma patients, displaying an impressive AUC of 0.9. This performance surpassed that of the Braden scale, highlighting stress hormones as superior objective assessment indicators for future API evaluations and aiding in clinical risk assessments. Further analysis revealed a notable decrease in INS levels within the API group, coupled with increased levels of Glu, Cort, and FBG. This observation strongly suggests a close and intricate relationship between stress hormones and the occurrence of API.

Notably, Glu, Cort, and FBG exhibited an upward trend as API worsened, followed by a subsequent decrease after treatment. These outcomes provide further evidence of the intimate relationship between stress hormones and API, underscoring their crucial clinical evaluation implications. This observation aligns with the findings of a prior study.

Changes in Stress Hormones Before and After Treatment

In comparison with the baseline (pre-treatment), the API group exhibited increased levels of INS after treatment, while Glu, Cort, and FBG decreased (P < .05). This suggests that as the condition of API improves, there are corresponding changes in the levels of stress hormones, see Figure 5.
Conducted by Wu et al., reinforcing the consistency of our results. The automatic activation of the patient's stress response post-trauma leads to the substantial release of stress hormones, offering a comprehensive understanding of their dynamic impact on API progression and treatment response.

An illustrative example is the consequential increase in FBG, which can induce persistent pathological hyperglycemia in the patient's body. This elevated glucose level serves as a catalyst for the accelerated reproduction of bacteria in vivo, triggering infections that can severely compromise the skin microcirculation system and subsequently lead to the onset of API.

Simultaneously, hyperglycemia contributes to vascular neuropathy, particularly evident in conditions such as lower limb vascular stenosis. Patients experiencing such vascular complications may exhibit lower skin temperatures and increased susceptibility of distal limbs to cold. The presence of whitish or dark purple (red) skin signals potential ischemia or hypoxia in local tissues, serving as a clinical indicator suggestive of the likelihood of API. We suggest that this phenomenon represents the primary mechanism through which stress hormones contribute to API.

Additionally, previous research has explored the use of a high-sugar INS mixture in the treatment of localized pressure sores. The underlying mechanism primarily involves INS enhancing the utilization rate of glucose, promoting protein synthesis, improving microvascular perfusion, and alleviating vasospasm. These findings strongly demonstrate the beneficial impact of INS supplementation on individuals dealing with pressure sores and API. However, the increased secretion of stress hormones in trauma patients hinders the normal metabolism of INS. This disturbance expedites the imbalanced secretion of FBG, causing an increased state of hyperglycemia. Concurrently, it reduces the perfusion capacity of blood vessels, thereby increasing the susceptibility to capillary hypoxia, ischemia, and necrosis.

We posit that with the increasing severity of trauma, the patient's stress response intensifies, leading to a more secretion of stress hormones. This heightened hormonal activity subsequently elevates the risk of API. The occurrence of API, in turn, triggers a reinforcement of the stress response in patients, establishing a cyclic pattern intertwined with the trauma experience. Consequently, as the treatment progresses, the stress hormone levels in patients within the API group tend to normalize, reflecting a positive trajectory towards recovery.

Therefore, we advocate for a future approach in dealing with trauma patients that involves the initial assessment of API risk through the monitoring of stress hormone levels. Subsequently, tailored nursing management strategies can be implemented, such as careful blood sugar control and the application of high-sugar INS mixtures on the contact areas between medical devices and the skin, aligning with the specific conditions of each patient. At the same time, essential measures, including ensuring the cleanliness and dryness of the patient's skin and promoting regular physical activities, should be implemented to proactively prevent the occurrence of API.

**Study Limitations and Future Directions**

The present study has certain limitations that warrant acknowledgement. The evaluation of short-term changes in stress hormone levels in API patients is confined by the relatively brief duration of this research. To comprehensively understand the trajectory of stress hormone alterations, an extended follow-up period becomes imperative. A more prolonged observation period would allow for a more accurate depiction of long-term variations and enhance the credibility and applicability of the findings. Furthermore, to meet the imperative need for greater representativeness and comprehensiveness in research outcomes, future investigations must incorporate a more expansive and diverse cohort of cases. Future studies should aim to explore the intricate relationship between a broader set of stress hormone indicators and API. The ultimate objective is to construct a robust and comprehensive risk prediction model. This model strives to offer the medical community a more reliable and clinically relevant reference for proactive and effective patient care.

**CONCLUSION**

In conclusion, stress hormones exhibit a close correlation with the occurrence of API in trauma patients. The detection of stress hormone levels emerges as a valuable tool for efficiently assessing the likelihood of API. This proactive approach enables timely preventive measures and interventions, ultimately diminishing the incidence of API and mitigating potential threats. The implications of this research extend beyond clinical outcomes, holding great significance in alleviating the physical and mental distress experienced by trauma patients. Moreover, the economic burden and strain on medical resources associated with API can be curtailed through early assessment and targeted interventions. This study underscores the critical role of stress hormone monitoring as a proactive strategy for enhancing patient outcomes and optimizing healthcare resource utilization.

**CONFLICTS OF INTEREST**

The authors report no conflict of interest.

**FUNDING**

None.

**AVAILABILITY OF DATA AND MATERIALS**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**REFERENCES**


